Egyptian Journal of Surgery Vol. (19), No. (1), Jan., 2000

ENDOCRINE PROFILE FOR OUTCOME PREDICTION IN MULTIPLE TRAUMATIZED CRITICALLY ILL PATIENT

By
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Major trauma is a pathophysiological state, which threaten the integrity of the internal environment causing alteration in the sympathoadrenal activity.The aim of this work was to study some endocrinal changes in multiple trauma critically ill patients, and to study the correlation between the level of the hormones and the severity of trauma.This study was conducted on 20 critically ill multitrauma patients with injury severity score more than 14 in addition to 10 healthy persons as a control group.The separated plasma was analysed for adrenaline, noradrenaline, cortisol, growth hormone, thyroxine, and tri-iodothyronine levels.There were significant elevation of plasma adrenaline, noradrenaline, and cortisol in all patients. Growth hormone level was elevated in the low risk group patients. There was significant decrease in plasma thyroxine (T3) and truodothyronine (T4) in all patients.T3 and cortisol can be taken in the first day in multiple trauma critically ill patients to predict their mortality and identify the quality of health care. Growth hormone and thyroid hormone replacement may be of value in trauma patients. Other endocrinal changes occur during trauma but need to be evaluated in further studies.

Key words:Multiple trauma, Critically ill patient, Injury severity score, Hormones

Abbreviations:Injury severity score (ISS), Adrenocorticotropic hormone (ACTH), Antidiuretic hormone (ADH), Triiodothyronine (T3), Thyroxine (T4), Thyroid stimulating hormone (TSH)

INTRODUCTION

Multiple injuries are recognized as two or more significant injuries in one body. There is a minimum number of lesions that an individual has to be considered a multiple injured patient. These lesions include severity of injury and the number of body areas involved in multiple injured individual [1]. The injury severity score (ISS) scored from 0 to 45, with higher scores indicating greater injury severity and mortality [2]. The critically ill trauma patient is any patient with at least one major injury and multiple minor injuries, with injury severity score (ISS) ranging from 14-45 points. The ISS was developed by Baker and coworkers in 1974 in an effort to quantify the effect of severity of injury and the number of body areas involved in multiple injured individual [3].

Major trauma is a pathophysiological state that threatens the integrity of the internal environment causing alteration in the sympathoadrenal activity. The biphasic nature of metabolic responses has been most intensively studied after injury. During the acute (or ebb) phase, defense of circulation is the chief priority and, a part from meeting that need the metabolic activity decreases. If the patient survives for hours or days, a recovery (or flow) phase ensues that may persist for weeks to months. At this time the metabolic activity increases above basal level to a degree dependent on the extent of injury [4].

Catecholamine mediated vasoconstriction, aided by activation of the renin-angiotensin-aldosteron system, is ap essential component of the defense against injury, but when prolonged, the same response can result in necrosis of vital organs and can potentiate the development of lactic acidosis from widespread tissue hypoxia. Catecholamines in addition, may be involved in the pathogenesis of stress ulceration and paralytic ileus after severe injury. Hyperglycemia in the acute phase after injury is due to interaction of epinephrine, glucagon and cortisol [5,6]. Trauma activates the hypothalamic-pituitary-adrenal axis

resulting in increased plasma ACTH and cortisol levels. A decreased blood volume stimulates ADH secretion. Pain and nausea may be even stronger stimuli to the secretion of ADH. Increased levels of growth hormones have been noted following injury, especially in the anabolic phase. However, a decreased GH level was noted in the catabolic phase of severe injury. The role of this primarily anabolic hormone in the catabolic "flow" phase is not known [7,8,9].

Trauma was reported to result in increase of protein-bound-iodine in some studies but not in the others. Although no increase in the serum T4 level was observed following trauma, serum T3 values were found to be decreased. Major trauma has a rapid, profound and long-lasting effect on gonadal activity, as judged from decreased testosterone levels, while the effect on adrenal steroids is less pronounced [10,11].

PATIENT & METHODS

This study was conducted on 20 critically ill multi-trauma patient, (In addition to 10 healthy persons as a control group), admitted at Mansoura Emergency Hospital in the period from January 1997 to June 1997, with injury severity score more than 14, their ages ranged between 18-44 years (with mean age 28.3 y). They were 23 males and 7 females. According to the ISS, patients were divided into:
Group I: Patients with high risk group ISS>24 (10 Patients).
Group II: Patients with low risk group ISS (14-24) (10 Patients).
Group III: Control group 10 (patients).

Every patient was subjected to the followings: -
- Thorough history, including time and type of trauma, method of transportation, and maneuvers done to the patient.
- Full clinical examination.
-Laboratory investigations, including:- (A) Routine investigations: liver function, serum creatinine, blood picture, blood glucose, serum electrolytes, serial blood gases. (B) Serum cortisol, adrenaline, noradrenaline, growth hormone, thyroxin, and truodothyronine.

- Blood samples were taken at three occasions, first on admission to the hospital after clinical evaluation, the second on the third day of admission to the hospital, and the third on the seventh day of admission to the hospital. Venous blood was taken into three polypropylene tube (5 ml) containing EDTA and transferred in ice to the laboratory as soon as possible for separation of plasma. The separated plasma was divided into aliquots and kept at -800C till time of analysis of cortisol, adrenaline, noradrenaline, growth hormone, thyroxine, and truodothyronine.

RESULTS

Age & Sex:

This study comprised 30 patients, 23 males, and 7 females. Based on ISS, they were divided into high- risk group (10 patients), low risk- group (10 patients), and a control groups (10 patients). Their ages ranged between 18-44 y (with mean age 28.3 y).

Clinical presentation

The mean value of ISS in high risk group was 31.9, and in low risk group was 19.1.

Descriptive data

Five patients developed multiple organ failure, 1 of the low risk group representing 10% of cases, and 4 cases of the high risk group representing 40% of cases.

Four patients with multiple organ failure died; one patient in the low risk group and 3 patients in the high risk group.

Hormonal level at the day of entry (Table1):

Adrenaline, noradrenaline, and cortisol showed significant increase in patients of the group I and group II, versus the control group ($p<0.001$). Growth hormone showed a significant increase in patients with low risk group versus the high risk group and the control group ($p<0.001$). T3 & T4 showed a significant decrease in patients of the group I and group II versus the control group ($p<0.001$) (Fig 1).

Hormonal variation according to the day of samDlina (Table 2):

Adrenaline, noradrenaline, and cortisol showed a significant increase at day 1 and day 3, while they showed significant decrease at day 7 in both groups ($p<0.01$). Growth hormone showed insignificant changes in its level according to the day of sampling in both groups ($p>0.05$). T3 & T4 showed insignificant changes in its level according to the day of sampling in both groups ($p>0.05$) (Fig2).

Laboratory data among studied group according to degree of risk (Table 3):

Adrenaline showed no significant difference between high risk group and low risk group as regard the day of sampling ($p>0.05$).

Noradrenaline showed no significant difference between high risk group and low risk group at day 1, and day 7 ($p>0.05$), while it showed significant increase in the high risk group at day 3 ($p<0.05$) (Fig3).

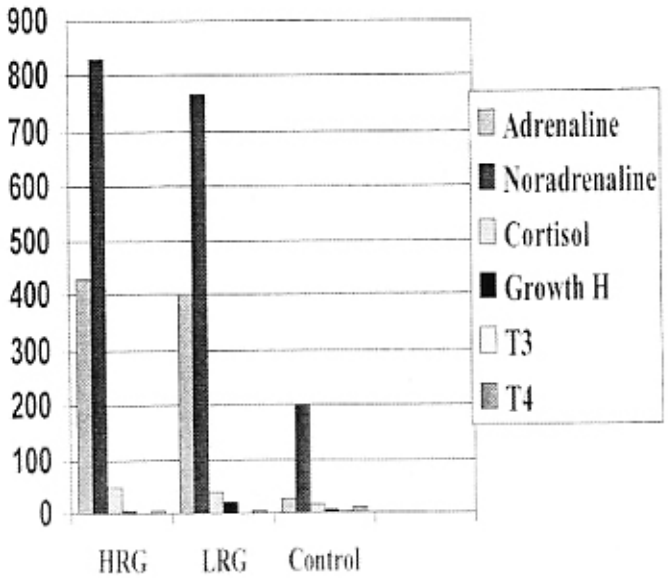
Cortisol showed no significant difference between high risk group and low risk group at day 1 ($p>0.05$), while it showed significant increase in the high risk group at day 3 and day 7 ($p<0.05$).

Growth hormone showed a significant decrease in the high risk group at days I ,3,and 7 ($p<0.05$).

T3 and T4 showed no significant difference between high risk group and low risk group as regard day of sampling ($p>0.05$).

Table (1):*Comparison between hormonal level at the day of entry between HRG, LRG, and control group.*

Hormone	*HRG*	*LRG*	*Control gp*	*F test*	*P*
Adren (pg/ml)	428±108.4	401.5±95.38	27±13.37	73.07	<0.001
Norad (pg/ml)	831±102.36	767.5±119	200±51.8	124.9	<0.001
Cortisol (μ/dl)	50.2±14.67	38.8±17.72	14.9±8.99	14.46	<0.001
GH (μlU/ml)	5.24±9.46	20.5±8.64	4.13±3.03	18.9	<0.001
T3 (ng/dl)	1.09±0.55	1.17±0.45	1.83±0.38	8.43	<0.001
T4 (μg/dl)	5.72±2.33	6.43±2.29	9.68±1.61	10.17	<0.001



(Fig 1) Comparison between hormonal level at the day of entry in HRG, LRG, and Control group

Table (2): ***Hormonal variation according to the day of sampling***

Hormone	*Day*	*LRG*	*HRG*
Adrenaline	1	401.50±95.38	428.00±108.40
	3	439.75±68.49	474.00±66.87
	7	236.50±95.27	291.60±113.73
Noradrenaline (pg/ml)	1	767.50±119.28	831.00±102.36
	3	742.30±73.40	797.00±47.15
	7	386.50±79.62	388.50±64.29
Cortisol (μg/dl)	1	38.80±17.72	50.20±14.07
	3	33.35±8.62	40.00±8.80
	7	13.80±7.08	25.40±9.64
Growth H (μlU/ml)	1	20.05±8.67	5.24±9.46
	3	18.80±7.68	4.72±2.55
	7	20.04±5.71	9.29±7.11
T3 (ng/dl)	1	1.17±0.45	1.09±0.65
	3	1.32±0.41	1.23±0.49
	7	1.51±0.35	1.36±0.52
T4 (μg/dl)	1	6.43±2.29	5.72±2.33
	3	7.16±2.62	6.12±1.93
	7	7.15±2.36	6.47±1.91

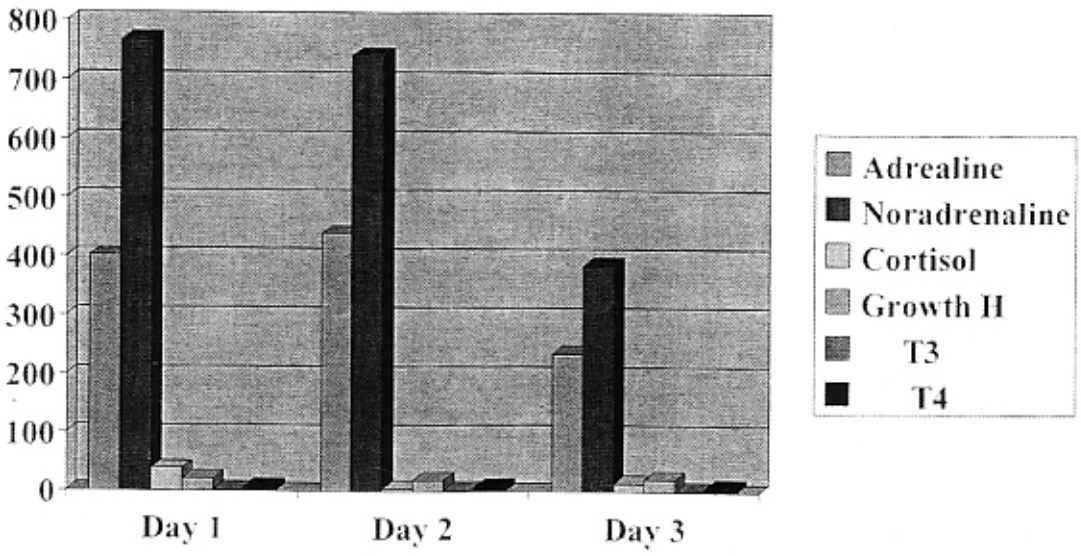


Fig 2 Hormonal variation according to the day of sampling in LRG

Table (3): ***Laboratory data among studied group according to degree of risk:***

Hormone	*Day*	*LRG (mean±SD)*	*HRG (mean±SD)*	*t*	*P*
Adrenaline	1	401.5±95.38	428±108.4	0.69	>0.05
(pg/ml)	3	439.75±68.49	474±66.87	1.3	>0.05
	7	236.5±95.27	291.6±113.7	1.4	>0.05
Nor adrenaline	1	767.5±119.28	831±102.36	1.44	>0.05
(pg/ml)	3	742.3±73.4	797±47.15	2.14	<0.05
	7	386.5±79.62	388.5±64.29	0.07	>0.05
Cortisol (µg/dl)	1	38.8±17.72	50.2±14.07	1.77	>0.05
	3	33.35±8.62	40±8.8	1.98	<0.05
	7	13.8±7.08	25.4±9.61	3.95	<0.05
Growth H	1	20.05±8.67	5.24±9.46	-4.28	<0.05
(µlU/ml)	3	18.8±7.68	4.27±2.55	-7.42	<0.05
	7	20.04±5.71	9.29±7.11	-4.48	<0.05
T3 (ng/dl)	1	1.17±0.45	1.09±0.56	-0.45	>0.05
	3	1.32±0.41	1.23±0.49	-0.58	>0.05
	7	1.51±0.35	1.36±0.52	-0.94	>0.05
T4 (µg/dl)	1	6.43±2.29	5.72±2.33	0.79	>0.05
	3	7.16±2.62	6.12±1.93	-1.11	>0.05
	7	7.15±2.36	6.47±1.91	-0.78	>0.05

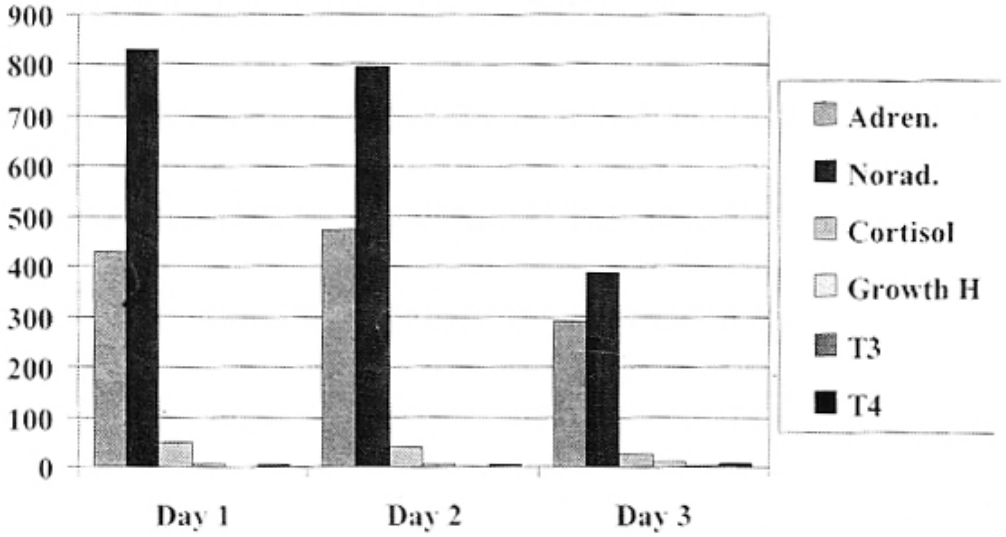


Fig 3 Hormonal variation according to the day of sampling in HRG

DISCUSSION

Activation of the sympathetic nervous system is a well-recognized part of the stress response to injury, and may contribute to patient morbidity by precipitating hypermetabolism, cardiac arrhythmia and pulmonary hypertension. Stimulation of the hypothalamo-pituitary-adrenal axis by injury leads to release of several mediators including: Catecholamine, ACTH, and cortisol, which initiate hypermetabolic state to maintain blood volume and tissue perfusion to meet the body demand. Plasma Catecholamine in patients suffering from head injury without systemic trauma reflects the severity of neurological dysfunction [12].

Hormonal responses to trauma are bi-directional, functional derangement includes increase in Adrenocorticotropic hormone, cortisol hormone, growth hormone, and prolactin hormone levels. In contrast, gonadotropin, gonadal steroids, and thyroid hormone concentration decrease [13].

In this work there was significant elevation of plasma adrenaline, noradrenaline, and cortisol in all patients on admission when compared with the control group. Also their level were correlated positively with ISS. One week after the injury their levels decreased but not to the control level. Petreson et al., 1993, found elevated plasma adrenaline and noradrenaline following multiple trauma, with significant correlation between global measurement of trauma (ISS) and Catecholamine blood level especially in patients with head trauma and brain injuries [14]. Woolf et al. 1990, reported that plasma noradrenaline did not change significantly during the first 48 hours while plasma adrenaline decreased with time in patients multisystem trauma with or without head injury [15]). Jeevanandam et al.1992, reported high plasma cortisol levels in patients with severe multiple injuries with high injury severity score. Bessy and Lowe 1993 stated that ACTH, and cortisol response to trauma is proportional to the extent of injury [16]. Barton etal.1987 reported that the magnitude and duration of plasma cortisol level has been related to patient outcome [17].

In this work there was significant elevation of plasma growth hormone in low risk group patients when compared with the high risk group and the control group. Increased level of growth hormone has been noted following injury, especially in the anabolic phase. The utility of growth hormone in reversing catabolism post-injury appears to be clinically dependent on adequate caloric intake. Melarvie et al. 1995 found that basal level of the anabolic growth hormone is significantly decreased in critically ill trauma patients, pulsatile GH bursts persist in the injured patients during day and night [18].

Altered thyroid hormone with severe stress and critical illness is another well-recognized finding. The euthyroid sick syndrome has become established as a distinct syndrome, demonstrating the effect of critical illness on thyroid function. In this work there was significant decrease in plasma T3 &T4 in all patients on admission when compared with control group. Ziegler et al.1990, found that serum T3 and T4 decreased in all patients suffering from traumatic injury irrespective of the presence or absence of head injury [19]. Some studies showed reliability of thyroid hormone replacement in multiple trauma patients, others failed to demonstrate the beneficial effects of thyroid hormone treatment [20,21].

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